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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,974	06/04/2001	Mathew A. Von Wronski	2238-7	6852

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,974	VON WRONSKI ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,23-36 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,23-36 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In the Office Action of 3/25/2004, the Examiner noted that "Additionally, Applicant was telephoned in order to specifically elect the specific composition as the invention (not species) drawn to elected invention of Group I. During a telephone conversation with Scott McNees on 3/2/2004 a provisional election was made with traverse to prosecute the invention of Formula I (A-L-B), wherein *A is a monomer and specifically TKPPR*; L is any linker; and B is the substrate phospholipids." Although Applicant has amended the claims to be drawn to phospholipids specifically, as the elected invention's substrate B; Applicant has not so amended monomer A to be limited to the elected invention (TKPPR only). The claims still read on TKPPR and any analogue of TKPPR, the latter of which falls outside the elected invention. Again, it is noted at the outset, that all pending claims, namely claims 1, 23-36, and 49, have only been searched and examined on the merits as being drawn to the elected composition (and specifically only TKPPR as the monomer A).

Claim Rejections - 35 USC § 112 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 23-36, and 49, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 23-36, and 49, the claims remain unclear, since they are still drawn to a monomer of TKPPR *or a TKPPR analogue*. Specifically, it is unclear what would constitute the structure of any TKPPR analogue? The only arguable description of what would constitute such an analogue that could be found in specification ¶'s 33, 40, and 95; describing a preferred embodiment of a "TKPPR tetramer". However, the specification never defines what the structure of such a tetramer is (i.e. which amino acid residues form it), or even defines that such a tetramer is a "TKPPR analogue". It is suggested that Applicant amend the claims to be drawn to the elected monomer A "TKPPR", by deleting the phrase "or a TKPPR analogue".

Claim Rejections - 35 USC § 112 1st Scope of Enablement

Claims 1, 23-36, and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide TKPPR as monomer A, does not reasonably provide enablement for any analogue of TKPPR as monomer A, in the invention's composition or method of ultrasound imaging. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is

proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the use of any TKPPR analogue in the composition or method of ultrasound imaging.

The nature of the invention: The invention is drawn to a composition which comprises a compound of formula (I) [A-L-B], wherein A is a monomer of TKPPR *or a TKPPR analogue* (among other structural characteristics).

The state of the prior art and the predictability or lack thereof in the art:

Amino acids range from common amino acids, to uncommon amino acids, and even "important amino acids, such as the neurotransmitter y aminobutyric acid, that have no relation to proteins." (Online-Medical Dictionary. "Amino acid". http://cancerweb.ncl.ac.uk/cgi-bin/omd?query=amino+acid. 13 Nov. 1997). An analogue is defined as "A compound that is structurally similar to another" (Online-Medical Dictionary. "Analogue". http://cancerweb.ncl.ac.uk/cgi-bin/omd?analogue. 10 Jan 1998).

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The only arguable description of what would constitute such an analogue that could be found in specification ¶'s 33, 40, and 95; describing a preferred embodiment of a "TKPPR tetramer". However, the specification never defines what

the structure of such a tetramer is (i.e. which amino acid residues form it), or even defines that such a tetramer is a "TKPPR analogue". Thus, there are an innumerable number of potential peptide fragments, and amino acid substitutions (conservative or non-conservative), that could chemically alter/be synthesized into the peptide TKPPR; however, Applicant has not clearly described a single one of these "analogues".

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to a composition which comprises a compound of formula (I) [A-L-B], wherein A is a monomer of TKPPR *or a TKPPR analogue*. With the substantial variability among what such an "analogue" could structurally be defined as; it is not clear as to what may be included in the invention as claimed. Absent sufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement on the use of any analogue of TKPPR in the composition or method of ultrasound imaging of the present invention; it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 23-36, and 49 under 35 U.S.C. 103(a) as being unpatentable over Pollak (US 5,789,555) in view of Barbera-Guillem (US 6,252,664), is maintained for the reasons of record. Applicants' arguments have been fully considered but are not found persuasive.

As discussed in the first action, Pollak teaches monomer TKPPR (col. 3, lines 61-65; SEQ ID NO: 1) conjugated to a linker (e.g., col. 4, lines 51-67 to col. 5, lines 1-10) and any

substrate that is "insoluble and inert in labeling solutions and can be functionalized with a linking group" (which "phospholipids" are categorizable in)(e.g., col. 4, lines 34-50). Additionally, Pollak also teaches a method of using this composition for diagnostic/radiodiagnostic imaging (e.g., col. 1, lines 12-32; col. 5, line 56)(see entire specification). However, Pollak, although teaching that *any* substrate that is "insoluble and inert in labeling solutions and can be functionalized with a linking group" may be used in the composition (which would encompass the characteristics of elected "phospholipids"), does not expressly teach the use of "phospholipids" as the substrate in the composition.

Barbera-Guillem teaches the use of phospholipids as substrates (col. 5, lines 6-7 and 19) in imaging compositions (abstract).

Applicant first argues that Pollak does not teach Applicants' claimed compositions. This is not found persuasive, because as indicated, Pollak teaches the use of monomer A TKPPR, connected to a linker and broadly any substrate (wherein Barbera-Guillem (also drawn to the field of imaging technology) is cited simply as a secondary reference, merely to indicate that phospholipids were known substrates, at the time of Pollak and at the time of Applicants' invention). Absent evidence to the contrary that the specific substrate "phospholipid" has embellished monomer A TKPPR (a known core compound/peptide for imaging compositions) with some unexpected result; there is motivation for someone to use the substrate phospholipid of Barbera-Guillem as the "any" substrate of Pollak. Applicant secondly argues that Pollak does not teach Applicants' method of *ultrasound* imaging using the above-described composition. This is also not found persuasive because Applicants' own specification (¶ 9) defines that the invention is applicable to the entire range of "imagining" techniques; namely "[t]he imaging

techniques, as used herein, include X-ray Imaging, Magnetic Resonance Imaging, Light Imaging, Scintigraphy, and Ultrasound Echograpy." Thus, like Applicant, Pollak also contemplated use of the composition in diagnostic/radiodiagnostic imagining (even if not expressly naming "ultrasound" imaging, per se).

Again, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use "phospholipids" as the substrate of Pollak, because Barbera-Guillem teaches the advantageous use of phospholipids as substrates in imaging compositions; and because Pollak [teach] that *any* substrate that is "insoluble and inert in labeling solutions and can be functionalized with a linking group" may be used in the composition (which would encompass the characteristics of elected "phospholipids").

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Applicant's amendment (as well as lack thereof regarding the elected invention, monomer only "TKPPR") necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA
9/16/04

CHRISTOPHER R. TATE
PRIMARY EXAMINER